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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/421,971	10/20/1999	FRED H. GAGE	SALK2350	4863

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/421,971	Applicant(s) GAGE ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 23-60 were cancelled, and claim 1 was amended in Paper No. 14, 9/16/2002. Claims 1-11, 13-22 are pending and under consideration.

Response to Amendment

The rejections of the cancelled claims are rendered moot, and thus withdrawn.

The rejection of claims 1-11, 13-22 under 35 U.S.C. 112, first paragraph has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 1-11, 13-22 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,265,173 (Evans et al.) has been obviated by Applicant's amendment, and is thus withdrawn.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13-22, 52-54 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record set forth in Paper No. 12, 3/12/2002.

Claim 1 is vague and indefinite in the recitation of the term "functional entity". There is no indication in the claim as to what function the protein must have. Therefore, the metes and bounds of the claim cannot be determined. Claims 2-11, 13-22, 52-54 are rejected insofar as they depend on the recitation in claim 1 of "functional entity". Applicant argues that the term is clear in light of the specification, and that the claim has been amended to recite four types of

functions which the chimeric proteins are contemplated to possess. However, it is not clear whether the functions added to the claim refer to the "functional entity" or to the "functional protein unit", thus the metes and bounds of the claim still cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-5, 14, 19, 22 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,830,462 (Crabtree et al.).

The '462 patent discloses materials, methods and applications relating to the oligomerizing of chimeric proteins with a dimeric or multimeric organic molecule materials for utilizing protein homodimerization, heterodimerization and oligomerization in living cells. Chimeric responder proteins are intracellularly expressed as fusion proteins with a specific receptor domain. Treatment of the cells with a cell permeable multivalent ligand reagent which

binds to the receptor domain leads to dimerization or oligomerization of the chimeras. The chimeric proteins are designed such that oligomerization triggers the desired subsequent events, e.g. the propagation of an intracellular signal via subsequent protein-protein interactions and thereby the activation of a specific subset of transcription factors (column 2, lines 29-42).

The '462 patent discloses chimeric proteins having a binding domain and an action domain, where the binding domain and action domain are in the nucleus, such that ligand-mediated oligomerization of the protein, by itself (to form a homo-oligomer) or with a different fused protein comprising a different action domain (to form a hetero-oligomer), induces initiation of transcription directly via complexation of the oligomer(s) with the DNA transcriptional initiation region column 11, lines 30-39), thus claims 1-4, 22 are anticipated. The chimeric proteins are not necessarily mammalian (column 4, lines 37-38), thus claim 5 is anticipated. The '462 patent gives examples of dimerized protein include the estrogen receptor (column 23, lines 1-5), thus claim 14 is anticipated. The chimeric proteins will have a C-terminal domain, thus claim 19 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 13-14, 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,830,462 (Crabtree et al.) in view of U.S. Patent No. 6,265,173 (Evans et al.).

The '462 patent discloses materials, methods and applications relating to the oligomerizing of chimeric proteins with a dimeric or multimeric organic molecule materials for utilizing protein homodimerization, heterodimerization and oligomerization in living cells. Chimeric responder proteins are intracellularly expressed as fusion proteins with a specific receptor domain. Treatment of the cells with a cell permeable multivalent ligand reagent which binds to the receptor domain leads to dimerization or oligomerization of the chimeras. The chimeric proteins are designed such that oligomerization triggers the desired subsequent events,

e.g. the propagation of an intracellular signal via subsequent protein-protein interactions and thereby the activation of a specific subset of transcription factors (column 2, lines 29-42).

The '462 patent discloses chimeric proteins having a binding domain and an action domain, where the binding domain and action domain are in the nucleus, such that ligand-mediated oligomerization of the protein, by itself (to form a homo-oligomer) or with a different fused protein comprising a different action domain (to form a hetero-oligomer), induces initiation of transcription directly via complexation of the oligomer(s) with the DNA transcriptional initiation region column 11, lines 30-39); examples of dimerized protein include the estrogen receptor (column 23, lines 1-5).

The '462 patent does not disclose insect receptor proteins. The '173 patent discloses multimeric receptor species that belong to the steroid/thyroid superfamily of receptors, comprising at least one member of the steroid/thyroid superfamily of receptors and the ultraspiracle receptor (column 3, lines 22-27). The ultraspiracle receptor is insect derived. A multimeric receptor comprising the ecdysone receptor is disclosed (column 5, lines 29-30). A multimeric receptor comprising the dimerization domain of the ultraspiracle protein is disclosed (column 3, lines 27-60). Multimeric receptors comprising RXR receptors, glucocorticoid receptors, mineralocorticoid receptors etc. are disclosed (column 5, lines 20-46). The multimeric receptor would have a C terminal domain, thus claim 19 is anticipated. The hinge domain is optional. The multimeric receptor comprises an activation domain (column 5, lines 47-60).

Therefore, it would have bben obvious to one of skill in the art at the time the invention was made to make chimeric fusion protein as taught in the '462 patent using RXR receptors or insect receptors as taught in the '173 patent. The motivation is provided in the '462 patent which

discloses that intracellular crosslinking of chimeric proteins by synthetic ligands has potential in basic investigation of a variety of cellular processes and in regulating the synthesis of proteins of therapeutic or agricultural importance. Furthermore, ligand mediated oligomerization permits regulated gene therapy. In so doing, it provides a fresh approach to increasing the safety, expression level and overall efficacy obtained with gene therapy (column 2, lines 56-64).

Conclusion

Claims 1-11, 13-22 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 12, 2002

DAVID S. ROMEO
PRIMARY EXAMINER